

WE CLAIM:

1. A DNA vaccine suitable for eliciting an immune response against cancer cells comprising a polynucleotide construct operably encoding a 5 *Fra-1* protein and IL-18 in a pharmaceutically acceptable carrier.
2. The DNA vaccine of claim 1 wherein the polynucleotide construct is operably incorporated in a vector.
3. The DNA vaccine of claim 2 wherein the vector is an attenuated bacterial vector.
4. The DNA vaccine of claim 3 wherein the attenuated bacterial vector is selected from the group consisting of attenuated *Salmonella typhimurium*, *Salmonella typhi*, *Shigella*, *Bacillus*, *Lactobacillus*, *BCG*, *Escherichia coli*, *Vibrio cholerae*, and *Campylobacter*.
5. The DNA vaccine of claim 4 wherein the attenuated bacterial vector is an attenuated *Salmonella typhimurium*.
6. The DNA vaccine of claim 5 wherein the attenuated *Salmonella typhimurium* is a doubly attenuated *aroA⁻ dam⁻* *S. typhimurium*.
7. The DNA vaccine of claim 1 wherein the polynucleotide construct encodes a *Fra-1* protein having an amino acid sequence selected from the 20 group consisting of SEQ ID NO: 2 and SEQ ID NO: 4.
8. The DNA vaccine of claim 1 wherein the polynucleotide construct encodes IL-18 having an amino acid sequence selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 8.
9. The DNA vaccine of claim 1 wherein the polynucleotide construct comprises a polynucleotide encoding a human or murine *Fra-1* protein, and having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 3.
10. The DNA vaccine of claim 1 wherein the polynucleotide construct comprises a polynucleotide encoding a human or murine IL-18, and having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 30 5 and SEQ ID NO: 7.

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11. The DNA vaccine of claim 1 wherein the polynucleotide construct further encodes IL-12.

12. The DNA vaccine of claim 1 wherein the polynucleotide construct operably encodes a polyubiquitinated Fra-1 protein.

5 13. The DNA vaccine of claim 12 wherein the polynucleotide construct is operably incorporated in a vector.

14. The DNA vaccine of claim 13 wherein the vector is an attenuated bacterial vector.

10 15. The DNA vaccine of claim 14 wherein the attenuated bacterial vector is selected from the group consisting of attenuated *Salmonella typhimurium*, *Salmonella typhi*, *Shigella*, *Bacillus*, *Lactobacillus*, *BCG*, *Escherichia coli*, *Vibrio cholerae*, and *Campylobacter*.

16. The DNA vaccine of claim 15 wherein the attenuated bacterial vector is an attenuated *Salmonella typhimurium*.

15 17. The DNA vaccine of claim 16 wherein the attenuated *Salmonella typhimurium* is a doubly attenuated *aroA⁻ dam⁻ S. typhimurium*.

18. The DNA vaccine of claim 12 wherein the polynucleotide construct encodes a Fra-1 protein having an amino acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 4.

20 19. The DNA vaccine of claim 12 wherein the polynucleotide construct encodes IL-18 having an amino acid sequence selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 8.

25 20. The DNA vaccine of claim 12 wherein the polynucleotide construct comprises a polynucleotide encoding a human or murine Fra-1 protein, and having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 3.

21. The DNA vaccine of claim 12 wherein the polynucleotide construct comprises a polynucleotide encoding a human or murine IL-18, and having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 5 and SEQ ID NO: 7.

30 22. The DNA vaccine of claim 12 wherein the polynucleotide construct further encodes IL-12.

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23. The DNA vaccine of claim 1 wherein the polynucleotide construct comprises an Fra-1 polynucleotide having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, and SEQ ID NO: 3 and an IL-18 polynucleotide having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 5, and SEQ ID NO: 7.

5 24. The DNA vaccine of claim 23 wherein the DNA construct is operably incorporated in an attenuated *Salmonella typhimurium* vector.

10 25. The DNA vaccine of claim 24 wherein the attenuated *Salmonella typhimurium* is a doubly attenuated *aroA⁻ dam⁻* *S. typhimurium*.

15 26. A method of inhibiting tumor growth in a mammal comprising the step of administering to the mammal an effective immunological response eliciting amount of a DNA vaccine comprising a polynucleotide construct operably encoding a Fra-1 protein and IL-18 in a pharmaceutically acceptable carrier, whereby the mammal exhibits an immune response elicited by vaccine and specific to tumor cells.

27. The method of claim 26 wherein the polynucleotide construct encodes a Fra-1 protein having an amino acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 4.

20 28. The method of claim 26 wherein the polynucleotide construct encodes IL-18 having an amino acid sequence selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 8.

25 29. The method of claim 26 wherein the polynucleotide construct comprises a polynucleotide encoding a human or murine Fra-1 protein, and having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 3.

30 . 30 . The method of claim 26 wherein the polynucleotide construct comprises a polynucleotide encoding a human or murine IL-18, and having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 5 and SEQ ID NO: 7.

31. The method of claim 26 wherein the Fra-1 is polyubiquitinated.

32. The method of claim 26 wherein the mammal is a human.

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33. The method of claim 26 wherein the polynucleotide construct is operably incorporated in an attenuated bacterial vector.

34. The method of claim 33 wherein the attenuated bacterial vector is selected from attenuated *Salmonella typhimurium*, *Salmonella typhi*,
5 *Shigella*, *Bacillus*, *Lactobacillus*, *BCG*, *Escherichia coli*, *Vibrio cholerae*, and *Campylobacter*.

35. The method of claim 33 wherein the attenuated bacterial vector is an attenuated *Salmonella typhimurium*.

36. The method of claim 35 wherein the attenuated *Salmonella typhimurium* is a doubly attenuated *aroA*⁻ *dam*⁻ *S. typhimurium*.
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37. The method of claim 33 wherein the vaccine is administered orally.

38. An article of manufacture comprising a vaccine of claim 1 packaged in a hermetically sealed, sterile container, the container having a label
15 affixed thereto, the label bearing printed material identifying the vaccine and providing information useful to an individual administering the vaccine to a patient.

39. An isolated plasmid vector comprising a polynucleotide construct operably encoding a polyubiquitinated Fra-1 protein.
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40. The plasmid vector of claim 39 wherein the Fra-1 protein is a human or murine Fra-1 protein.

41. The plasmid vector of claim 39 further comprising a polynucleotide construct operably encoding IL-18.

42. The plasmid vector of claim 41 wherein the IL-18 is a human or murine IL-18.
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43. A transformed host cell transfected with a polynucleotide construct operably encoding a Fra-1 protein and IL-18.

44. The transformed host cell of claim 43 wherein the polynucleotide construct operably encodes polyubiquitinated Fra-1 protein.
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45. The transformed host cell of claim 43 wherein the Fra-1 protein is a human or murine Fra-1 protein.

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46. The transformed host cell of claim 43 wherein the IL-18 is human or murine IL-18.

47. The transformed host cell of claim 43 wherein the host cell is a prokaryotic cell.

5 48. The transformed host cell of claim 43 wherein the host cell is a eukaryotic cell.

49. The transformed host cell of claim 43 wherein the host cell is an attenuated bacterium.

10 50. The transformed host cell of claim 49 wherein the attenuated bacterium is selected from the group consisting of attenuated *Salmonella typhimurium*, *Salmonella typhi*, *Shigella*, *Bacillus*, *Lactobacillus*, *BCG*, *Escherichia coli*, *Vibrio cholerae*, and *Campylobacter*.

51. The transformed host cell of claim 49 wherein the attenuated bacterium is an attenuated *Salmonella typhimurium*.

15 52. The transformed host cell of claim 51 wherein the attenuated *Salmonella typhimurium* is a doubly attenuated *aroA⁻ dam⁻ S. typhimurium*.

20 53. A method of vaccinating a mammal against cancer, the method comprising the step of administering to the mammal an effective immunological response eliciting amount of a DNA vaccine comprising a polynucleotide construct operably encoding a Fra-1 protein and IL-18 in a pharmaceutically acceptable carrier, whereby the mammal exhibits an immune response elicited by vaccine and specific to tumor cells.

54. The method of claim 53 wherein the polynucleotide construct operably encodes a polyubiquitinated Fra-1 protein.

25 55. The method of claim 53 wherein the polynucleotide construct is operably incorporated in an attenuated bacterial vector.

30 56. The method of claim 55 wherein the attenuated bacterial vector is selected from the group consisting of attenuated *Salmonella typhimurium*, *Salmonella typhi*, *Shigella*, *Bacillus*, *Lactobacillus*, *BCG*, *Escherichia coli*, *Vibrio cholerae*, and *Campylobacter*.

57. The method of claim 55 wherein the attenuated bacterial vector is an attenuated *Salmonella typhimurium*.

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58. The method of claim 57 wherein the attenuated *Salmonella typhimurium* is a doubly attenuated *aroA⁻ dam⁻* *S. typhimurium*.

59. The method of claim 53 wherein the mammal is a human.

60. The method of claim 53 wherein the vaccine is administered
5 orally.

61. A method of delivery of genetic material to a mammalian cell *in vivo* comprising orally administering to a mammal doubly attenuated *aroA⁻ dam⁻* *S. typhimurium* cells comprising a polynucleotide construct operably encoding a therapeutically useful gene product.

10 62. The method of claim 61 wherein the therapeutically useful gene product is a tumor antigen capable of eliciting an immune response in the mammal against tumor cells.

15 63. The method of claim 61 wherein the therapeutically useful gene product is an immune stimulating molecule capable of stimulating the immune system of the mammal.

64. The method of claim 61 wherein the therapeutically useful gene product comprises a tumor antigen capable of eliciting an immune response in the mammal against tumor cells and an immune stimulating molecule capable of stimulating the immune system of the mammal.

20 65. The method of claim 63 wherein the tumor antigen is a Fra-1 protein and the immune stimulating molecule is IL-18.